PUBLIC HEALTH COMMUNICATION CENTRE AOTEAROA

A single shot to prevent cancer? HPV vaccine can!

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Summary

The human papillomavirus (HPV) vaccine is woefully under-used in Aotearoa New Zealand (NZ). This is despite its excellent safety profile and evidence that it prevents cancer. Added to the NZ immunisation schedule in 2008, coverage has yet to reach the original 75% target. The World Health Organization now recommends a 1-dose vaccine schedule for 9-20-year-olds. Forty countries, including Australia and UK now follow this advice. NZ continues to follow the manufacturer datasheet (2-dose schedule), despite the science. Thus we waste scarce resources (vaccinator and vaccine) and give an extra injection of minimal, if any, value to our youth. This non-evidence-based obstacle needs to be removed. A single dose to prevent cancer helps promote HPV vaccine. We should aim for at least 90% coverage and eliminate HPV-related cancers from NZ.

In this Briefing, we describe a missed opportunity to change the School Year 8 HPV immunisation programme from a 2-dose to a 1-dose schedule. A barrier is the manufacturer datasheet that specifies a 2-dose schedule. However, health authorities can address this barrier. A single dose helps coverage. With increased promotion we can achieve at least 90% coverage and eliminate cervical cancer and other cancers caused by HPV vaccine-types.

The virus and vaccine

Infection with human papillomavirus (HPV) is common. A modelling study estimated over 80% of USA adults were infected by age 45 years.[1] HPV spreads through skin-to-skin contact, including intimate sexual contact. The infection does not usually cause symptoms and most people clear the virus. But in some people the virus remains, and can cause warts and later cancer in the affected area: particularly cervical cancer, other anogenital cancers, and head and neck cancer.

The HPV vaccine is highly effective with an excellent well-established safety profile. It also indirectly protects the unvaccinated by reducing spread. Data on its efficacy in preventing cervical cancer are now emerging. For example, a Scottish study reported no cases of invasive cancer in women aged 24 to 32 years who had received at least one dose at age 12 or 13 years of age.[2] (See Appendix 1 for more on the virus and vaccine.)

In 2020, the World Health Assembly adopted the Global Strategy for cervical cancer elimination, targeting 90% HPV coverage in females and screening. A technical assessment suggested eradication of HPV (vaccine-types) is possible with 90% coverage in all sexes; 95% in higher risk groups.[3]

New Zealand experience

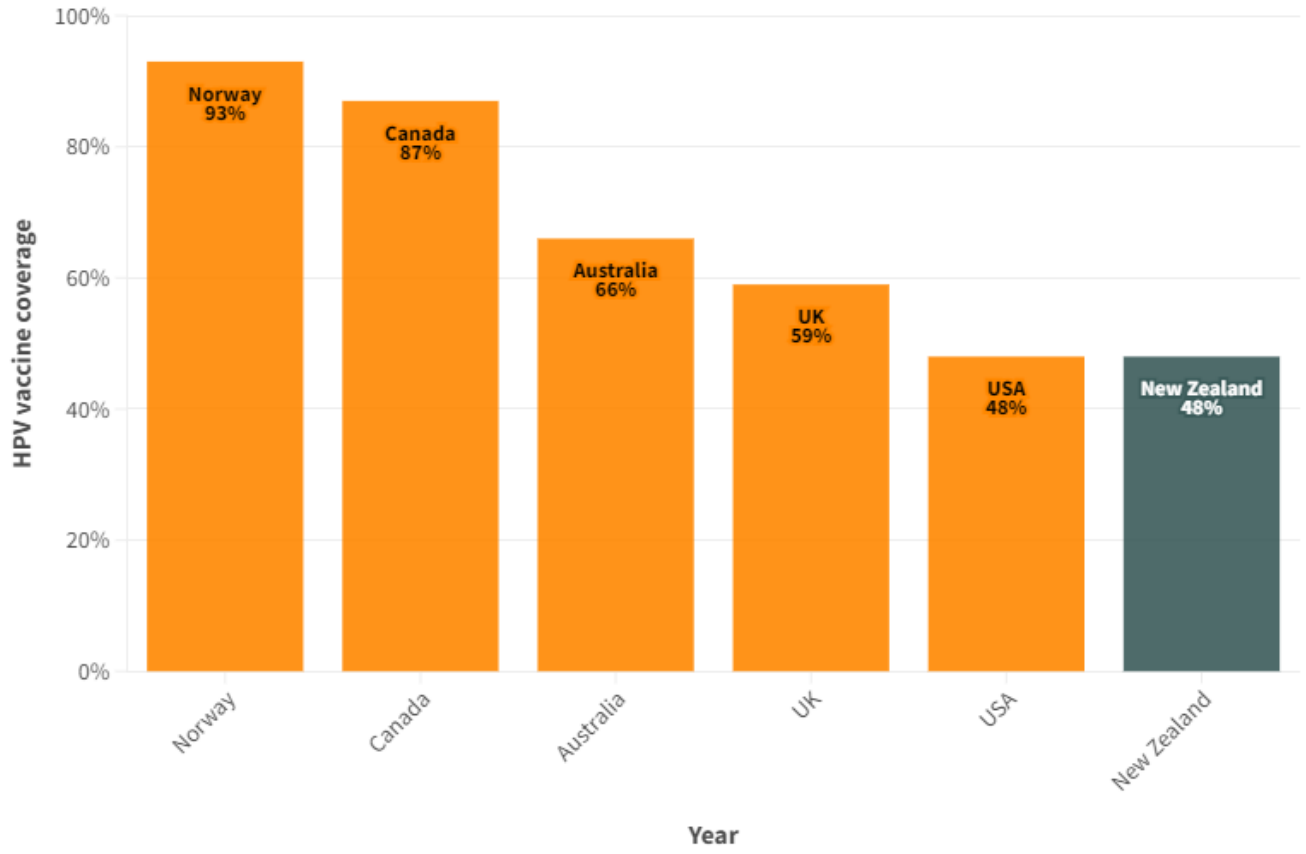
HPV vaccine was first used in NZ in 2008 in a 3-dose schedule for 17 or 18 year-old females. In 2009, it was extended to females born from 1992 onwards. After a two-year catch-up for all female students in Years 8 to 13, it was offered as an annual programme for Year 8 girls (age ~12 years).[4]

In 2014, the World Health Organization (WHO) recommended changing to a 2-dose schedule, as data emerged to show it was just as effective as 3-doses for ages 9-14 years.[5]

NZ changed to a 2-dose schedule in 2017. The reduction in doses made it more affordable and cost-effective to include males in the programme from 2017.

The WHO monitors HPV coverage in 9-14 year females. For the latest year, 2021, NZ had lower coverage than Australia, UK and many developing countries. Even the USA, with a lower coverage previously matched that of NZ in 2021. Coverage has decreased in recent years, especially in Māori and Pacific peoples. (See Appendix 2 for NZ coverage data.)

Figure 1. HPV coverage for New Zealand and selected countries (2021)



Source: WHO Global Health Observatory
2021 HPV immunisation coverage estimates among primary target cohort (9-14 years old girls)

Time to move to a one-dose schedule

In 2022, the WHO recommended "an off-label option, a single-dose schedule can be used in girls and boys aged 9–20 years" based on "comparable efficacy and duration of protection as a 2-dose schedule".[6] The WHO noted a "potential risk of a lower level of protection if efficacy wanes over time, although there is no current evidence of this."

In the UK, the same conclusion was independently reached by their Joint Committee on Vaccination and Immunisation. The WHO HPV vaccine dashboard shows that 40 countries now have a 1-dose schedule; including Australia and England, who changed in 2023, despite no changes in their data sheets.

Historically, NZ vaccine policies have deviated from manufacturer data sheets. The Medsafe data sheet for the vaccine, in section 4.2 on dosage also states that its use "should be in

accordance with official recommendations." This allows health authorities to change to a single dose schedule, without changes to the data sheet – as other countries have done.

Improving HPV immunisation coverage

We need to improve coverage to get the full cancer-prevention benefits of the vaccine. Moving from a 2 to a 1-dose schedule for HPV vaccination makes increasing coverage easier, at it makes it more attractive to youth and their parents. Reviews have identified a range of measures to improve HPV coverage.[7,8,9]

We propose a deliberative democratic process, such as a citizen jury (advocated by the Department of the Prime Minister and Cabinet and the Public Service Commission) to adjudicate on options to increase coverage, including the consent process for school-based HPV immunisation. A written consent is currently required, leaving some children unprotected because a consent form was not returned, even though parental consent would have been given.

What this Briefing adds

- The HPV vaccine is highly effective with an excellent safety profile. It has reduced genital warts and is preventing cervical cancer. The potential to eliminate cervical cancer and other HPV-related cancers (eg, head and neck cancers) beckons.
- The vaccine was initially introduced with a 3-dose schedule, but new evidence shows one vaccine dose is adequate; already adopted by the UK and Australia.
- It took three years for NZ to change from 3-dose to a 2-dose schedule for HPV vaccine. Delaying the change to a 1-dose wastes tax-payer funds and health resources for limited, if any, benefit.

Implications for policy and practice

- Immunisation policies must be based on science, and not constrained by out-dated vaccine manufacturer datasheets.
- With a single dose, it becomes more feasible to set and achieve a 90% coverage target that can eliminate HPV-related cancers.
- Promotion of the vaccine becomes easier when only one dose is needed; ongoing efforts are needed to promote the vaccine and address misinformation.

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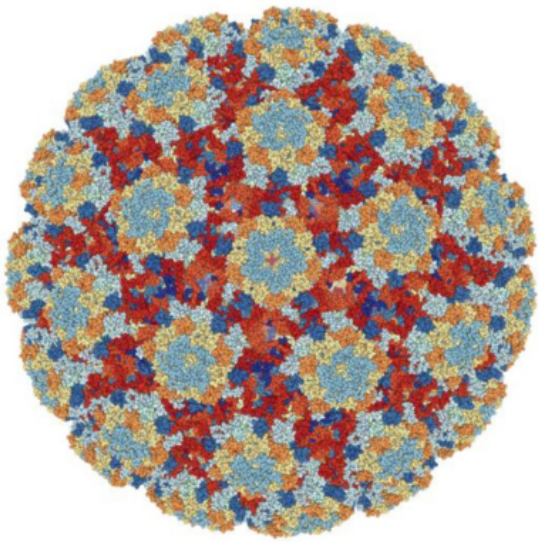
Appendix 1: Human papillomavirus (HPV) and its vaccine



It looks like the virus, but this is an image of the vaccine from its co-inventor.[10] The vaccine is made of L1 protein. This is one of two proteins that are the virus 'coat'. As it does not contain the DNA of a virus, it cannot infect. But it looks so much like the virus, it makes the vaccine work really well.

How do we make the proteins come together just like the virus? It's biology! They just naturally form ('self-assemble') into a set of five (pentamers) and 72 of these form a 20-sided shell

Several viruses are known to cause cancer. Human papillomavirus (HPV) causes the most. In 2018, 4% of all new cancers globally were HPV-related,[11] down from 4.5% in 2012.[12] In this appendix, we provide more details on the vaccine and its impact to date in preventing genital warts and cancer; and the cancer burden it can prevent.

HPV vaccine: from four to nine types

There are over 200 types of HPV, over 40 infect genital areas. Of these, 14 types are defined as 'high-risk' for causing cancer: HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66 and 68. The 'low risk' types rarely cause cancer, but some (6, 11, 42, 43, 44) cause

warts on or around the genitals, anus, mouth, or throat (about 90% from types 6 and 11). When warts form in the larynx or respiratory tract (respiratory papillomatosis) these can cause breathing problems.

The HPV vaccine first used in NZ had 4 types: 6, 11, 16, and 18. The first two cause about 90% of anogenital warts; the second two about 70% of cervical cancers and most other HPV-cancers. Since 2017, we have used nonavalent (ie, has 9 types) HPV vaccine that has five more high-risk HPV types, to cover 90% of cervical cancers.

HPV vaccine safety

Various adverse events following immunisation (AEFIs) with HPV vaccine have been highly publicised. The data and studies that fail to find the safety concern, not so much. Lack of trust is a related factor, fueled by disinformation.

An AEFI is indeed any event that occurs after immunisation. But these can be coincidental rather than being caused by the vaccine. A review of randomised studies found over a third had some health event after either vaccine (35%) or placebo (36%).[13] These events that follow equally after vaccine or placebo are coincidental that can be falsely blamed on the vaccine.

The WHO's Global Advisory Committee on Vaccine Safety (GACVS) has reviewed HPV vaccine safety several times, most recently in 2017. Aside from a risk of anaphylaxis in about 1.7 per million doses, and injection reactions including fainting (a common anxiety or stress-related reaction), no other adverse reactions have been identified. The GACVS concludes that "despite the extensive safety data available for this vaccine, attention has continued to focus on spurious case reports and unsubstantiated allegations... that have a demonstrable negative impact on vaccine coverage in a growing number of countries, and that this will result in real harm."

These findings are reinforced by reviews by the American Autonomic Society[14], a Cochrane Review of randomised trials[15], and a narrative review of 109 studies.[16]

HPV vaccine efficacy and impacts

In the initial studies, vaccine efficacy was 95% or higher in preventing persistent infection, cervical intraepithelial neoplasia (CIN) 2/3, and adenocarcinoma in situ (AIS).[4]

The Cochrane Library summarises the evidence for 'at least one dose' of HPV vaccine protecting against HPV16/18 pre-cancer and localised cancer of the cervix as 'high-certainty' and 'moderate-to high-certainty'. A 14 year follow-up study found no cases of pre-cancers from HPV16/18 in Nordic women, with no evidence of waning immunity over this time period.[17]

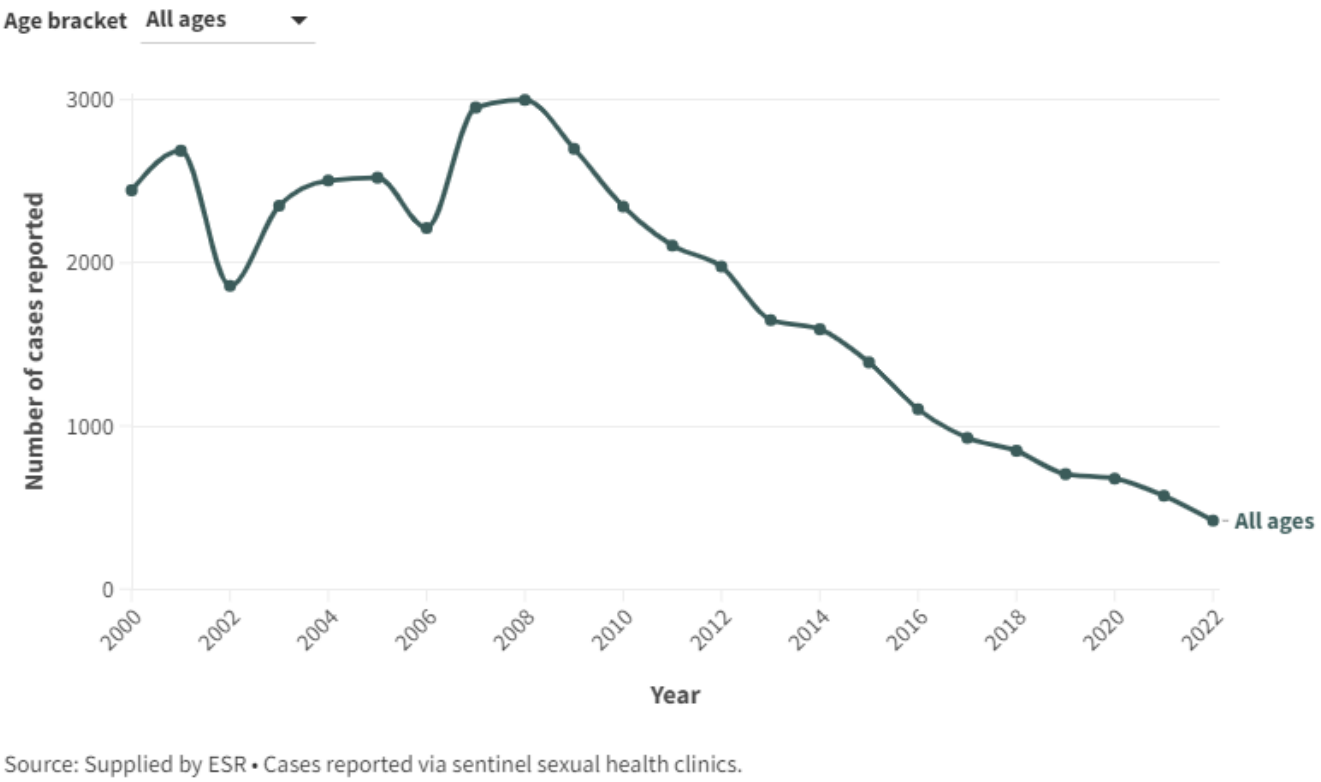
Data on **preventing cervical cancer** are just emerging. A Scottish study reported no cases of invasive cancer in women aged 24 to 32 years who had who received one or more doses at age 12 or 13 years of age.[2] Those given three doses at 14 to 22 years of age had cancer incidence: 3.2 vs 8.4 per 100,000 women who had no vaccine.

In Sweden, analysis of national register data on over 1.5 million females aged 10 to 30 years of age from 2006 through 2017 reported the vaccine 88% effective against invasive cervical cancer in those immunised under the age of 17 years.[18]

In England, a registry-based retrospective cohort study of 20-29 year old women reported 87%, 62% and 34% reductions in cancer incidence for those vaccinated at ages 12-13, 14-16, and 16-18 years, respectively.[19]

The **impact on genital warts** was immediately apparent. A systematic review reported HPV vaccine leading to up to 90% reduction in HPV 6/11/16/18 infection and genital warts.[20] The USA CDC report that genital warts declined by 88% and 81% among teen girls and young adult women, respecitively, compared to 2006 when the vaccine was introduced. In NZ, there continues to be a decline in in the reported incidence of genital warts. (Figure A1).

Figure A1: Number of genital warts cases reported at selected sentinel sites, 2000-2022

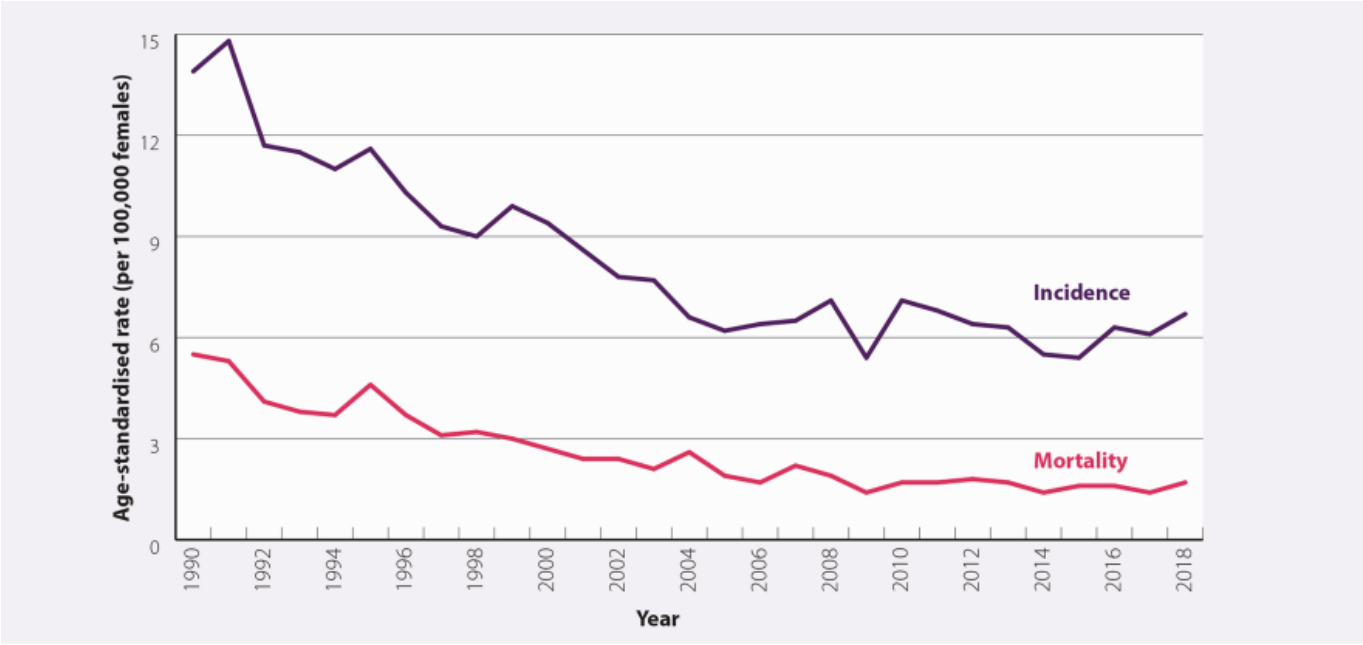


Source: Supplied by ESR • Cases reported via sentinel sexual health clinics.

New Zealand cancers

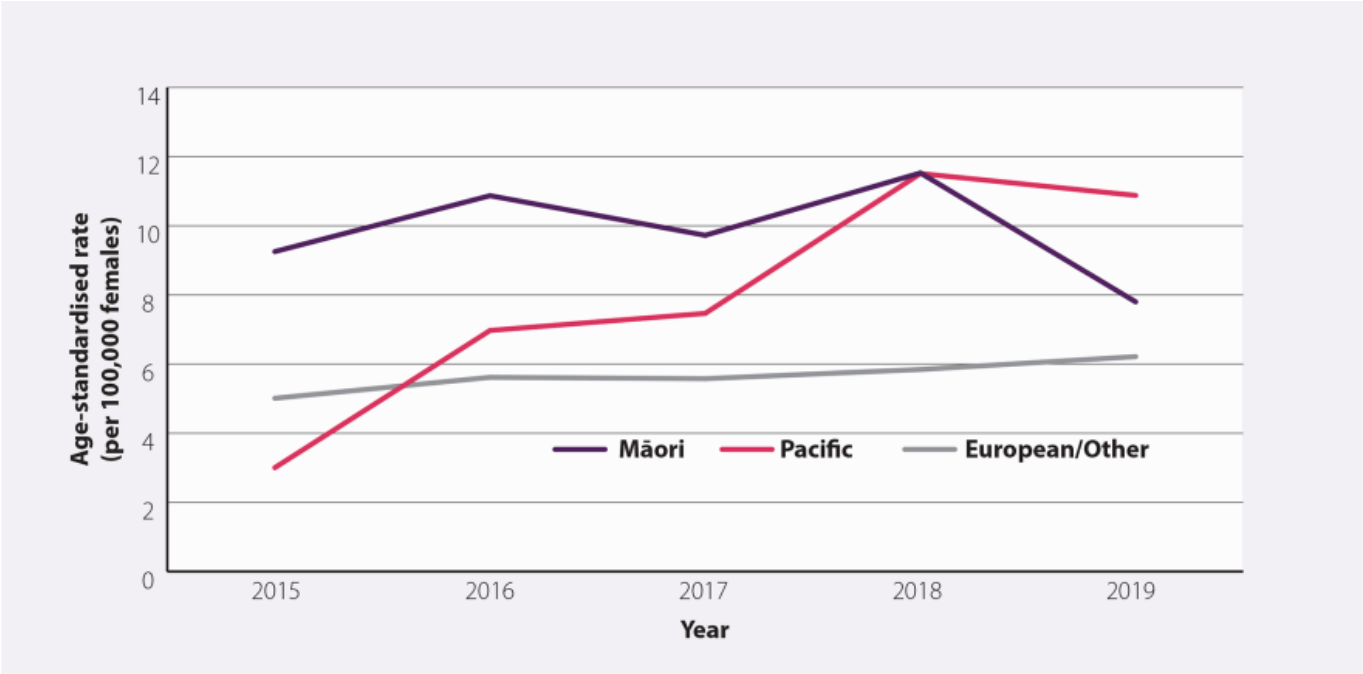
Analysis of cervical cancers in those born from 1990, the oldest vaccine-eligible females, has not been published for NZ. Cervical cancer incidence has been increasing since 2015, suggesting other factors are increasing incidence, while the declines from cervical screening had plateaued before the start of the programme in 2008 (Figure A2).

Figure A2: Age-standardised incidence and mortality rates (per 100,000 females) for cervical cancer between 1990 and 2018 in New Zealand. Source: bpacnz



The dip in 2009, the year after the start, is transient, suggesting a possible data issue. There seems to be a rise in incidence from 2015. The equity gap in cervical cancer, results from lower screening rates (Figure A3). Another inequity is that Māori have under double the incidence of cervical cancer, but over double (2.7) times the mortality.[4]

Figure A3. Age-standardised incidence rate (per 100,000 females) for cervical cancer by ethnicity between 2015 and 2019 in New Zealand. Source: bpacnz



Other cancers caused by HPV

There are no data on the impact of HPV vaccine on other cancers, but it is expected to prevent “about 69% of vulvar, 75% of vaginal, 63% of penile, 90% of anal and 70% of

oropharyngeal cancers."[4] Immunisation Handbook, Table 10.2 of the Handbook shows the incidence of 2017 HPV-related cancers, with most oropharyngeal cancers in the tonsil, and most of them in men:

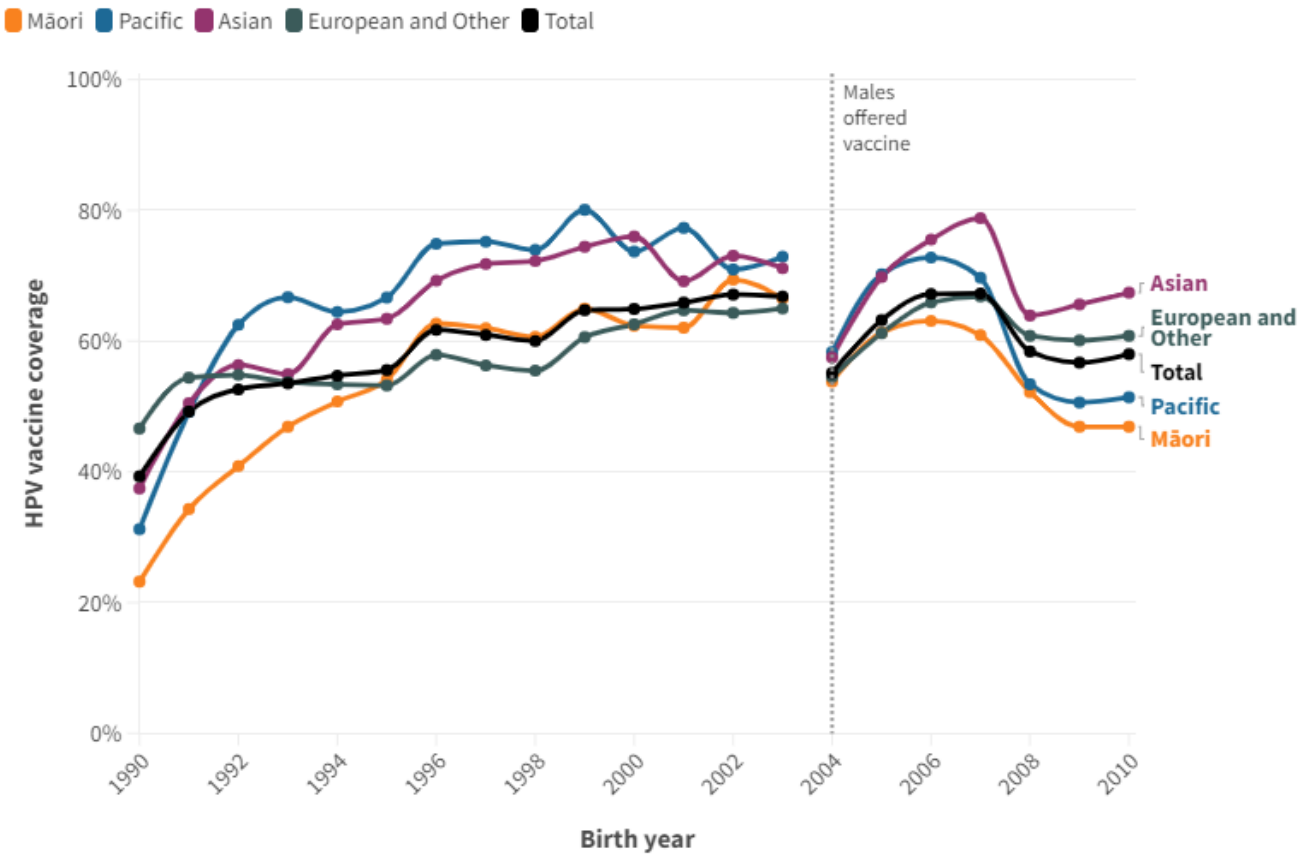
Table 1. Number and age-standardised rate (per 100,000) of HPV-associated cancers (excluding cervical), NZ, 2017[4]

Anatomic site	Number	Rate registrations (per 100,000)
Vulva	52	1.2
Vagina	19	0.5
Penis	18	0.5
Anus		
• women	40	1.1
• men	21	0.6
Oropharynx		
• women	4	0.1
• men	10	0.3
Tonsils		
• women	21	0.6
• men	85	2.7

Appendix 2: HPV immunisation coverage in NZ

HPV coverage is reported by birth cohort for females only until 2004 birth cohort. Coverage had been slowly improving until 2019 (2007 birth cohort), but dropped during the Covid-19 pandemic and may be recovering now (Figure A4).

Figure A4: HPV vaccine coverage by birth cohort and ethnicity



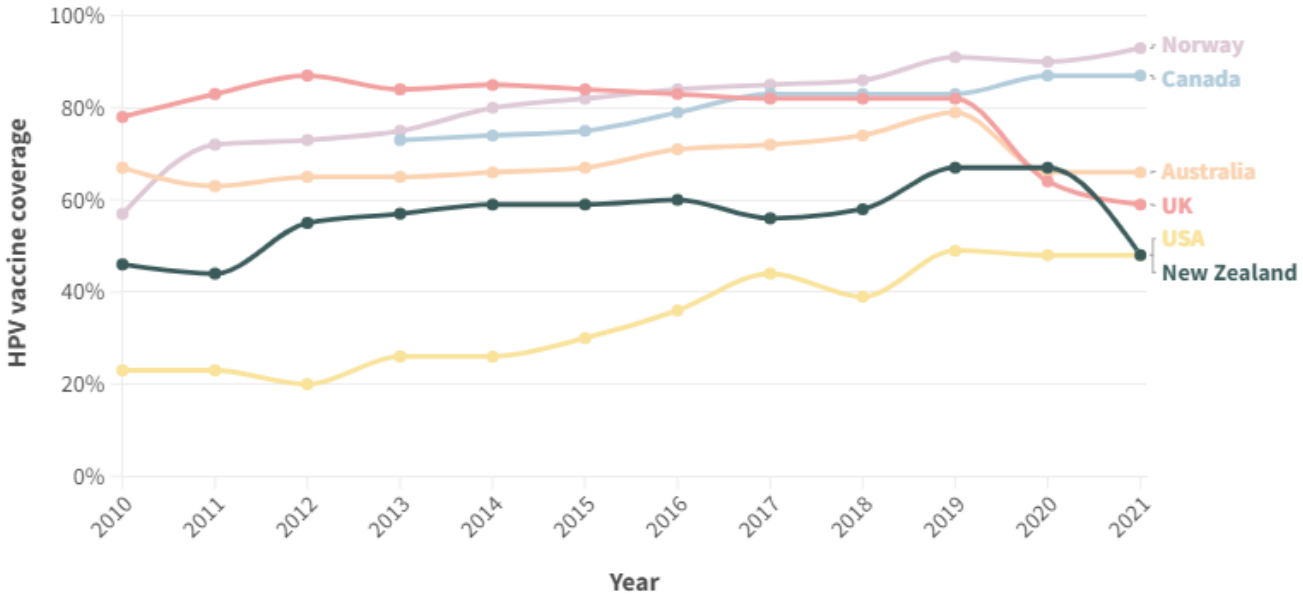
Source: Te Whatu Ora
Data for birth cohorts 1990-2003 includes only females. From 2004 coverage includes males and females.

The dip in coverage for the 2004 cohort reflects their age in 2017 when males became eligible (aged 13 years versus 12 years for most). But from the 2006 birth cohort, coverage for both sexes is practically the same.

The apparent negative ‘equity gap’ (1996 to 2003 birth cohorts) contrasts to that of childhood immunisation, though Asian ethnicities have the highest coverage for both. The equity gap for Māori emerges again with the pandemic (2008 cohort onwards), although remains smaller than in childhood immunisation.

WHO monitors HPV coverage in 9-14 year females. For the latest year, 2021, NZ had lower coverage than Australia, UK and many developing countries. Even the USA, with a lower coverage previously, matched that of NZ in 2021 (Figure A5).

Figure A5. HPV coverage, by year for New Zealand and selected countries



Source: WHO Global Health Observatory
HPV immunisation coverage estimates among primary target cohort (9-14 years old girls)

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